

CLAIMS

1. Process for preparing ursodeoxycholic acid di-sodium 3,7-disulfate comprising:
 - a) reacting ursodeoxycholic acid with sulfamic acid to give ursodeoxycholic acid di-ammonium 3,7-disulfate;
 - 5 b) treating the ursodeoxycholic acid di-ammonium 3,7-disulfate with organic sodium bases or inorganic sodium bases then treating the reaction mixture with an inorganic acid until a pH between 3.0 and 4.5 is reached to give ursodeoxycholic acid di-sodium 3,7-disulfate in solution.
2. Process as claimed in claim 1 wherein the reaction of stage a) is conducted in
10 an aprotic solvent.
3. Process as claimed in claim 2 wherein the aprotic solvent is N,N-dimethylformamide.
4. Process as claimed in claim 1 wherein the reaction of stage a) is conducted at a temperature between 40°C and 110°C.
- 15 5. Process as claimed in claim 4 wherein the temperature is between 80°C and 90°C.
6. Process as claimed in claim 1 wherein ursodeoxycholic acid di-ammonium 3,7-disulfate is separated from the reaction mixture of stage a) by fractional crystallisation with acetone.
- 20 7. Process as claimed in claim 1 wherein the inorganic sodium bases in stage b) are chosen from the group consisting of: sodium hydroxide, sodium carbonate and sodium bicarbonate.
8. Process as claimed in claim 7 wherein the organic sodium bases are sodium acetate.
- 25 9. Process as claimed in claim 1 wherein in stage b) the treatment of ursodeoxycholic acid di-ammonium 3,7-disulfate with organic sodium bases or inorganic sodium bases is conducted in alcoholic solvent.
10. Process as claimed in claim 9 wherein the alcoholic solvent is chosen from the group consisting of linear or branched lower C1-C4 alcohols or their mixtures.
- 30 11. Process as claimed in claim 10 wherein the alcohol is methanol.
12. Process as claimed in claim 1 wherein in stage b) the treatment with organic

sodium bases or inorganic sodium bases is conducted at a temperature between -10°C and 30°C .

13. Process as claimed in claim 12 wherein the temperature is between 0°C and 5°C .

5 14. Process as claimed in claim 1 wherein in stage b) the treatment with organic sodium bases or inorganic sodium bases is conducted under vacuum.

15. Process as claimed in claim 1 wherein in stage b) the acidification of the reaction mixture after treatment with organic sodium bases or inorganic sodium bases is conducted by treating the reaction mass with an inorganic acid chosen
10 from the group consisting of: hydrochloric acid, sulphuric acid, 85% (w/w) phosphoric acid or their mixtures.

16. Process as claimed in claim 15 wherein the acid is 85% phosphoric acid.

17. Process as claimed in claim 1 also comprising stage c), consisting in the recovery of ursodeoxycholic acid di-sodium 3,7-disulfate from the reaction
15 mixture, said stage comprising: c') removing, by filtration, precipitated inorganic salts formed after acidification treatment and c'') precipitating ursodeoxycholic acid di-sodium 3,7-disulfate from the filtrate whereby the solution containing ursodeoxycholic acid di-sodium 3,7-disulfate is concentrated by distillation and the residue is re-dissolved in organic solvent, preferably acetone, to isolate
20 ursodeoxycholic acid di-sodium 3,7-disulfate.

18. Process as claimed in claim 17 wherein in stage c') the filtration to remove the precipitated inorganic salts formed after acidification treatment is facilitated by treating the reaction mixture derived from stage b) with an organic solvent.

19. The process claimed in claim 18, wherein said organic solvent is acetone.

25 20. Process as claimed in claim 17 wherein in stage c'') the residue obtained by concentrating the solution containing ursodeoxycholic acid di-sodium 3,7-disulfate by distillation is re-dissolved in organic solvents, at a temperature between 20°C and 70°C , and the suspension thus obtained is then cooled to room temperature and filtered to obtain ursodeoxycholic acid di-sodium 3,7-disulfate as precipitate.

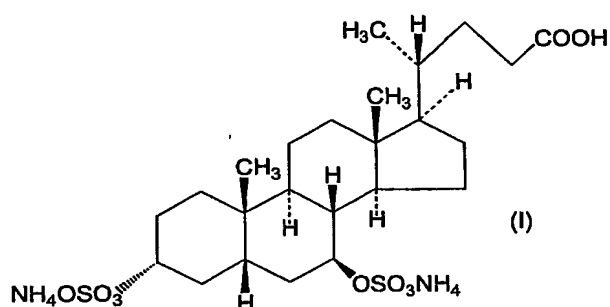
30 21. The process as claimed in claim 20, wherein said organic solvent is acetone and ursodeoxycholic acid di-sodium 3,7-disulfate is redissolved in said solvent at

a temperature comprised between 55° and 65°C.

22. Ursodeoxycholic acid di-ammonium 3,7-disulfate of formula:

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23. Process for synthesising ursodeoxycholic acid di-ammonium 3,7-disulfate comprising reacting ursodeoxycholic acid with sulfamic acid.

24. Process as claimed in claim 23 wherein the reaction with sulfamic acid is conducted in an aprotic solvent.

25. Process as claimed in claim 24 wherein the aprotic solvent is N,N-dimethylformamide.

26. Process as claimed in claim 23 wherein the reaction with sulfamic acid is conducted at a temperature between 40°C and 110°C.

27. Process as claimed in claim 26 wherein the temperature is between 80°C and 90°C.

28. Process as claimed in claim 23 wherein the ursodeoxycholic acid di-ammonium 3,7-disulfate is separated from the reaction mixture by fractional crystallisation with acetone.